AUG 21 2000

K001875

510(k) Summary of Safety and Effectiveness

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: _____

Applicant Information:

Date Prepared:	July 24, 2000
Name:	Diamedix Corporation
Address:	2140 N. Miami Avenue Miami, FL 33127
Contact Person:	Dr. Lynne Stirling
Phone Number:	305-324-2354
Fax Number:	305-324-2388

Device Information:

Trade Name:	Is-Rubella IgM Capture Test System
Common Name:	Rubella IgM EIA Test
Classification Name:	Enzyme linked immunosorbent assay, rubella (866.3510)

Equivalent Device:
CAPTIA Rubella-M

Device Description: The Is-Rubella IgM Capture Test System is an enzyme-linked immunosorbent assay (ELISA) for the qualitative detection of IgM to rubella in human serum

Intended Use: The assay is intended for use in detecting IgM antibodies to rubella antigen in human serum. The results of the assay can be used as an aid in the diagnosis of a current or recent infection with rubella.

Principle of the Procedure: The Is-Rubella IgM Capture Test System is based on the antibody-capture technique. Goat antibody against human IgM (u chain specific) is coated onto plastic microwells. Diluted samples are added to each well. Sample IgM antibodies are 'captured' and bind to the well. Specific IgM is detected by the additon of an immunocomplex consisting of rubella antigen linked to a mouse monocloncal anti-rubella antibody conjugated to horseradish peroxidase. After incubation and washing, a substrate solution is then added to each well. In the presence of bound enzyme, the substrate in converted to a blue colored product. After acid addition to stop the reaction, a yellow end product is formed that is read spectrophotometrically at 450 nm (reference 600-630 nm) and is directly proportional to the concentration of Rubella IgM in the sample.

SUMMARY OF SAFETY AND EFFECTIVENESS

Performance Characteristics

A. Comparison Testing

A total of four hundred and ninety-eight sera were tested for the presence of rubella IgM antibodies using the Diamedix Is-Rubella IgM Capture Test Kit and two other marketed tests at two independent sites, (site #1, California and site #2, New York) as well as Diamedix Corp., Miami, FL (site #3). At site #3 testing was performed both manually and using the MAGO Plus Automated EIA Processor.

Site #1, a large commercial laboratory in California, not affiliated with the manufacturer, tested 127 samples. These consisted of 101 fresh samples submitted to the laboratory for Rubella IgM testing and 26 frozen samples which had previously tested positive for Rubella IgM antibodies. Samples came from a variety of geographic locations and from patients with ages ranging from 1 day to 62 years old. For the fresh samples, 23 were from males and 77 from females. The remaining sample was not identified as regards gender. TABLE 1 compares the results obtained for the Is-Rubella IgM Capture Test Kit and their currently used EIA testing method.

Site #2, a commercial reference laboratory in New York, not affiliated with the manufacturer, tested 125 samples. These samples consisted of 50 fresh and 65 frozen samples submitted to the laboratory for Rubella IgM testing, as well as an additional 10 frozen samples procured from a vendor based on their supposed positive serostatus. Samples were obtained from various geographic regions and from patients with ages ranging from 2 years to 57 years old. Twenty-four samples were from males and ninety-six from females. The remainder were not identified as regards gender. Thirty-six of the females were identified as pregnant. TABLE 2 compares the results obtained for the Is-Rubella IgM Capture Test Kit and their currently used EIA testing method. TABLE 3 shows the performance for the pregnant female samples.

TABLE 1

Is-Rubella IgM Capture - Site #1

Other EIA	Positive	Negative	Equivocal
Positive	21	4	1
Negative	3	95	0
*Equivocal	0	3	0

*Overall Agreement 116/123 = 94.3% *95% CI*** 88.6 to 97.7%

TABLE 2

Is-Rubella IgM Capture - Site #2

Other EIA	Positive	Negative	Equivocal
Positive	7	13	0
Negative	2	102	1
*Equivocal	0	0	0

*Overall Agreement 109/124 = 87.9% *95% CI*** 82.2 to 93.6

TABLE 3: Pregnant Samples

Is-Rubella IgM Capture - Site #1

	Positive	Negative	Equivocal
Positive	2	3	0
Negative	2	29	0
*Equivocal	0	0	0

*Overall Agreement 31/36 = 86.1% *95% CI*** 70.5 to 95.3%

* Equivocal results were excluded from calculations ** 95% Confidence Intervals (CI) calculated by the Exact Method (9).

For Site #1, further resolution of the discordant samples was performed by testing such samples in a referee capture EIA method. Of the four samples that were negative in the Is-Rubella IgM Capture Test Kit and positive in the other EIA, three were negative and one was positive in the referee capture EIA method. The three samples positive in the Is-Rubella IgM Capture and negative in the other EIA were negative in the referee capture EIA.

For Site #2, further resolution of the discordant samples was performed in a similar manner. However, in this case, two referee test methods were used. The first was a capture EIA and the second was a non-capture EIA. Of the thirteen samples that were negative in the Is-Rubella IgM capture Test Kit and positive in the other EIA, nine were negative and four were positive in the capture EIA. For the non-capture EIA, all 13 samples were negative. For the two samples that were positive in the Is-Rubella IgM Test Kit and negative in the other EIA, both were negative in either referee method.

Note that the tabulated data were not recalculated after retesting of discordant samples

Site #3 (Diamedix Corp.) tested 246 samples (all frozen) by both the manual and the automated method. Of these samples 111 were from normal S. Florida blood donors. Fifty-six of the samples were obtained following an outbreak in the UK and were either serum pairs, seroconversion samples or had IgM detected by other methods. Fifty-five of the sera were from an outbreak in Japan. Seventeen sera were obtained post-vaccination and the remaining 7 sera were a commercially available seroconversion panel. TABLES 4 and 5 compare the results obtained for the Is-Rubella IgM Capture Test Kit and another marketed capture EIA method.

TABLE 4

Is-Rubella IgM Capture - Site #3 : Manual

Other EIA	Positive	Negative	Equivocal
Positive	94	3	6
Negative	6	127	1
*Equivocal	1	7	1

Overall Agreement 221/230 = 96.1% **95% CI 96.1-99.6

TABLE 5

Is-Rubella IgM Capture - Site #3 : MAGO Plus

Other EIA	Positive	Negative	Equivocal
Positive	100	2	1
Negative	5	126	3
*Equivocal	2	7	0

Overall Agreement 226/233 = 97.0 % **95% CI 97.8-100.0

* Equivocal results were excluded from calculations

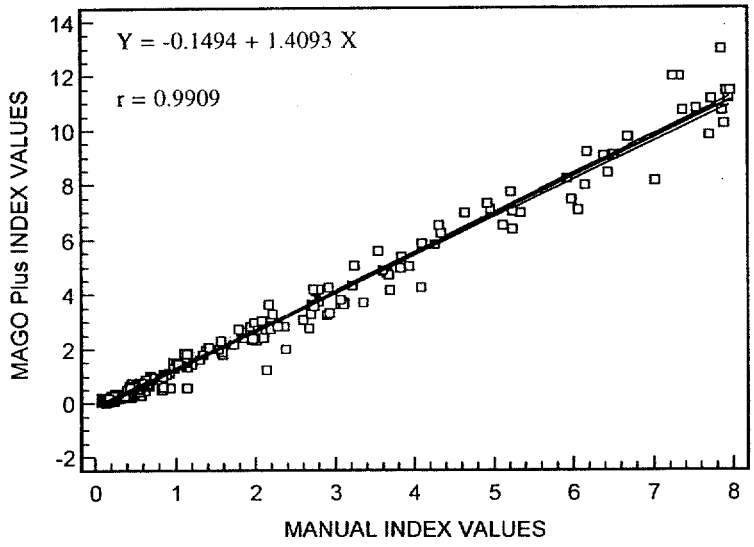
** 95% Confidence Intervals (CI) calculated by the Exact Method (9)

For Site #3 (manual testing), further resolution of the discordant sera revealed that of the 3 sera negative in the Is-Rubella IgM Capture Test Kit but positive in the other EIA, one was negative and two were positive by a referee EIA method. For the six sera positive in the Is-Rubella IgM Capture Test Kit and negative by the other EIA, 3 were positive and 3 were negative in the referee EIA. For MAGO Plus testing, of the two sera that were negative in the Is-Rubella IgM Capture Test Kit but positive in the other EIA, one was negative and one was positive in the referee EIA method. For the 5 sera that were positive in the Is-Rubella IgM Capture Test Kit and negative in the other EIA, 3 were positive and 2 were negative in the referee EIA.

B. Correlation of Manual and MAGO Plus Results

The Is-Rubella IgM Capture Test Kit has been developed for automated as well as manual use. To demonstrate the equivalence of the manual and MAGO Plus procedures, the results of the 246 samples tested above were compared. A scattergram and regression line of the results obtained with 95% confidence intervals is shown in FIGURE 1.

FIGURE 1 : Manual vs MAGO Plus Correlation



C. Cross-Reactivity Data

The specificity of the Is-Rubella IgM Capture Test Kit was verified by testing a number of sera containing relatively high levels of IgM antibody to other viruses as determined using commercially available test kits. A total of 25 known IgM-positive sera were tested. In addition, the effects of potential interference from rheumatoid factor (RF), anti-nuclear antibody (ANA), viral-specific IgG and heterophile antibodies were assessed by testing an additional 30 characterized sera. These data are shown in TABLE 6. TABLE 7 shows the lack of interference from samples containing high levels of IgG antibodies and low levels of IgM antibodies before and after removal of the IgG-class antibody.

TABLE 6

Specificity	# of Positve Samples	# Positive in Is-Rubella IgM Capture
EBV IgM	7	0
Lyme IgM	3	0
HSV IgM	5	0
CMV IgM	5	0
Toxoplasma IgM	5	0
Heterophile Antibody	4	0
RF	5	0
ANA	10	0
Rubella IgG	11	0

TABLE 7

Sample #	Before IgG Removal		After IgG Removal	
	IgG IU/ml	IgM Index	IgG IU/ml	IgM Index
1	48.9	2.389	0.0	2.071
2	46.2	1.585	0.0	1.382
3	55.3	2.499	0.0	2.359
4	35.8	2.829	0.0	2.567
5	44.5	2.053	0.0	1.788
6	38.7	2.027	0.0	1.737
7	36.4	1.826	0.0	1.613

IgG Pos $\geq$ 10 IU/ml IgM Pos $\geq$ 1.10

D. Verification of IgM Specificity

To confirm that the Is-Rubella IgM Capture Test Kit specifically detects IgM-class antibodies, twelve samples posititve for Rubella IgM in the Is-Rubella IgM Capture test Kit were treated with dithiothreitol (DTT) to destroy the IgM and were then retested in the Is-Rubella IgM Capture Test Kit. The results in TABLE 8 show that these samples were rendered negative following treatment with DTT confirming the specificity of the Is-Rubella IgM Capture Test Kit for detecting IgM-class antibodies.

TABLE 8

Sample #	Untreated		Treated with DTT	
	Is-Rubella IgM Capture		Is-Rubella IgM Capture	
	Index	Interp	Index	Interp
1	2.922	POS	0.227	NEG
2	4.683	POS	0.640	NEG
3	3.666	POS	0.418	NEG
4	3.278	POS	0.371	NEG
5	4.096	POS	0.565	NEG
6	4.872	POS	0.821	NEG
7	2.860	POS	0.394	NEG
8	4.384	POS	0.539	NEG
9	3.786	POS	0.499	NEG
10	2.325	POS	0.364	NEG
11	3.821	POS	0.628	NEG
12	1.736	POS	0.247	NEG

E. Precision

Six serum samples, as well as the kit Controls, were tested to assess the precision of the Is-Rubella IgM Capture Test Kit. Sites #1 and #2 tested samples in triplicate in three separate runs on three different days. Site #3 (Diamedix Corp.) tested samples in triplicate in two separate runs on three different days both manually and using the MAGO Plus Automated EIA Processor. The results obtained are shown in TABLES 9-12.

TABLE 9 : Site #1- Intra-Assay and Interassay Precision

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY (n=9)		
	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%
R1	0.185	0.01	5.41	0.220	0.01	4.55	0.195	0.05	25.64	0.200	0.029	14.50
R2	1.085	0.06	5.53	1.219	0.03	2.46	1.231	0.02	1.62	1.178	0.078	6.62
R3	1.590	0.12	7.55	1.588	0.08	5.04	1.490	0.04	2.68	1.556	0.088	5.66
R4	0.164	0.01	6.10	0.210	0.03	14.29	0.200	0.02	10.00	0.191	0.027	14.14
R5	2.547	0.24	9.42	2.645	0.14	5.29	2.460	0.10	4.07	2.551	0.168	6.59
R6	3.635	0.08	2.20	3.883	0.04	1.03	3.582	0.07	1.95	3.700	0.150	4.05
LPC	1.158	0.02	1.73	1.364	0.07	5.13	1.396	0.05	3.58	1.306	0.120	9.19
NC	0.262	0.01	3.82	0.273	0.00	3.66	0.245	0.01	4.08	0.260	0.013	5.00

TABLE 10 : Site #2 - Intra-Assay and Interassay Precision

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY (n=9)		
	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%
R1	0.277	0.04	14.44	0.288	0.06	20.83	0.435	0.10	22.99	0.333	0.097	29.13
R2	1.382	0.07	5.07	1.287	0.08	6.22	1.274	0.04	3.14	1.314	0.077	5.86
R3	1.722	0.15	8.71	1.431	0.15	10.48	1.574	0.08	5.08	1.576	0.170	10.79
R4	0.279	0.02	7.17	0.184	0.02	10.87	0.416	0.06	14.42	0.293	0.106	36.18
R5	2.330	0.02	0.86	2.042	0.19	9.30	2.531	0.15	5.93	2.301	0.246	10.69
R6	3.413	0.08	2.34	2.950	0.02	0.68	2.963	0.07	2.36	3.108	0.235	7.56
c/o CAL	0.944	0.03	3.18	0.719	0.06	8.34	0.901	0.04	4.44	0.854	0.110	12.88
LPC	1.168	0.04	3.42	1.195	0.12	10.04	1.281	0.18	14.05	1.215	0.121	9.96
NC	0.175	0.03	17.14	0.174	0.04	22.99	0.468	0.15	32.05	0.272	0.168	61.76

TABLE 11 : Site #3-Intra-Assay and Interassay Precision (Manual)

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY (n=18)		
	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%
A	0.315	0.073	23.17	0.268	0.029	10.82	0.250	0.017	6.80	0.278	0.052	18.71
B	0.275	0.070	25.45	0.213	0.026	12.21	0.208	0.042	20.19	0.232	0.056	24.14
C	1.247	0.028	2.25	1.220	0.066	5.41	1.251	0.070	5.60	1.240	0.056	4.52
D	1.487	0.109	7.33	1.626	0.120	7.38	1.588	0.187	11.78	1.567	0.147	9.38
E	2.179	0.120	5.51	2.209	0.167	7.56	2.027	0.077	3.80	2.138	0.144	6.74
F	4.195	0.231	5.51	4.359	0.480	11.01	4.549	0.504	11.08	4.368	0.425	9.73
c/o CAL	1.060	0.074	6.98	0.995	0.113	11.36	0.967	0.080	8.27	1.007	0.094	9.33
LPC	2.032	0.250	12.30	1.698	0.108	6.36	1.766	0.105	5.95	1.832	0.217	11.84
NC	0.246	0.063	25.61	0.163	0.039	23.93	0.167	0.021	12.57	0.192	0.057	29.69

TABLE 12 : Site #3- Intra-assay and Interassay Precision (MAGO Plus)

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY (n=18)		
	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%
A	0.17	0.046	27.06	0.16	0.054	33.75	0.17	0.040	23.53	0.17	0.04	23.53
B	0.15	0.034	22.67	0.17	0.034	20.00	0.14	0.021	15.00	0.15	0.03	20.00
C	1.35	0.078	5.78	1.39	0.055	3.96	1.38	0.091	6.59	1.37	0.07	5.11
D	1.99	0.218	10.95	2.32	0.270	11.64	2.21	0.234	10.59	2.17	0.27	12.44
E	3.10	0.296	9.55	3.64	0.200	5.49	3.42	0.352	10.29	3.38	0.36	10.65
F	4.39	0.269	6.13	4.64	0.272	5.86	4.41	0.288	6.53	4.48	0.28	6.25
c/o CAL	1.14	0.054	4.74	1.34	0.188	14.03	1.35	0.151	11.19	1.28	0.17	13.28
LPC	1.90	0.160	8.42	2.12	0.273	12.88	1.90	0.210	11.05	1.97	0.23	11.68
NC	0.15	0.029	19.33	0.13	0.036	27.99	0.14	0.024	17.14	0.14	0.03	21.43

Expected Values

The prevalence of rubella infection can vary depending on a number of factors such as age, gender, vaccination history, geographic location, socio-economic status, race, type of test used, specimen collection and handling procedures and clinical and epidemiological history of individual patients. In the present study two hundred sera from South Florida blood donors (102 female and 98 male) were evaluated in the Is-Rubella IgM Capture Test Kit. Of these samples, one hundred and ninety-five (97.5%) were negative, two (1%) were negative and three (1.5%) were equivocal. Comparable results were obtained using the MAGO Plus. TABLE 13 provides age distribution, geographic location and prevalence. FIGURE 2 shows a histogram showing the distribution of Index values obtained for this population. FIGURE 3 shows the distribution of Index values for the positive samples tested by Diamedix Corporation (See tables 4 and 5).

TABLE 13 : Age Distribution and Prevalence of Is-Rubella IgM in a Normal S. Florida Population

	Number of Donors	% Seronegative	% Seropositive	% Equivocal
Total Number	200			
Geographic Location: S. Fla	200	97.5% (195)	1.0% (2)	1.5% (3)
Age : 10-19	18	100.0% (18)	0.0% (0)	0.0% (0)
20-29	47	100.0% (47)	0.0% (0)	0.0% (0)
30-39	74	98.6% (73)	0.0% (0)	1.4% (1)
40-49	40	92.5% (37)	2.5% (1)	5.0% (2)
50-59	11	91.0% (10)	9.0% (1)	0.0% (0)
60-69	9	100.0% (9)	0.0% (0)	0.0% (0)
>70	1	100.0% (1)	0.0% (0)	0.0% (0)
Gender				
Males	98	97.0% (97)	2.0% (2)	1.0% (1)
Females	102	98.0% (98)	0.0% (0)	2.0% (2)

FIGURE 2: Distribution of Is-Rubella IgM Results in a Normal Population

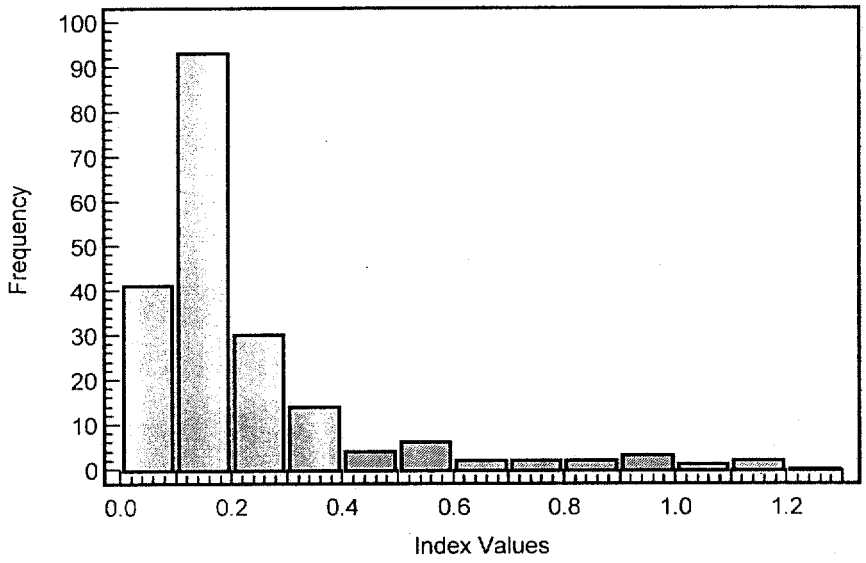
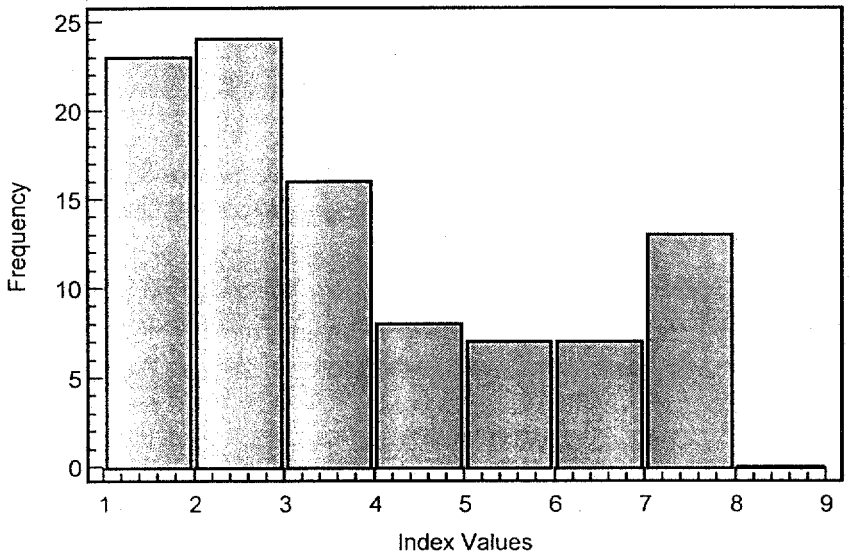


FIGURE 3: Distribution of Is-Rubella IgM Results in a Positive Population



C. Cross-Reactivity Data

The specificity of the Is-Rubella IgM Capture Test Kit was verified by testing a number of sera containing relatively high levels of IgM antibody to other viruses as determined using commercially available test kits. A total of 25 known IgM-positive sera were tested. In addition, the effects of potential interference from rheumatoid factor (RF), anti-nuclear antibody (ANA), viral-specific IgG and heterophile antibodies were assessed by testing an additional 30 characterized sera. These data are shown in TABLE 6. TABLE 7 shows the lack of interference from samples containing high levels of IgG antibodies and low levels of IgM antibodies before and after removal of the IgG-class antibody.

TABLE 6

Specificity	# of Positve Samples	# Positive in Is-Rubella IgM Capture
EBV IgM	7	0
Lyme IgM	3	0
HSV IgM	5	0
CMV IgM	5	0
Toxoplasma IgM	5	0
Heterophile Antibody	4	0
RF	5	0
ANA	10	0
Rubella IgG	11	0

TABLE 7

Sample #	Before IgG Removal		After IgG Removal	
	IgG IU/ml	IgM Index	IgG IU/ml	IgM Index
1	48.9	2.389	0.0	2.071
2	46.2	1.585	0.0	1.382
3	55.3	2.499	0.0	2.359
4	35.8	2.829	0.0	2.567
5	44.5	2.053	0.0	1.788
6	38.7	2.027	0.0	1.737
7	36.4	1.826	0.0	1.613

IgG Pos $\geq$ 10 IU/ml IgM Pos $\geq$ 1.10

D. Verification of IgM Specificity

To confirm that the Is-Rubella IgM Capture Test Kit specifically detects IgM-class antibodies, twelve samples posititve for Rubella IgM in the Is-Rubella IgM Capture test Kit were treated with dithiothreitol (DTT) to destroy the IgM and were then retested in the Is-Rubella IgM Capture Test Kit. The results in TABLE 8 show that these samples were rendered negative following treatment with DTT confirming the specificity of the Is-Rubella IgM Capture Test Kit for detecting IgM-class antibodies.

TABLE 8

Sample #	Untreated		Treated with DTT	
	Is-Rubella IgM Capture		Is-Rubella IgM Capture	
	Index	Interp	Index	Interp
1	2.922	POS	0.227	NEG
2	4.683	POS	0.640	NEG
3	3.666	POS	0.418	NEG
4	3.278	POS	0.371	NEG
5	4.096	POS	0.565	NEG
6	4.872	POS	0.821	NEG
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9	3.786	POS	0.499	NEG
10	2.325	POS	0.364	NEG
11	3.821	POS	0.628	NEG
12	1.736	POS	0.247	NEG

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

AUG 21 2000

Lynne Stirling, Ph.D.
Vice President of Quality Unit/Regulatory Affairs
Diamedix Corporation
2140 North Miami Avenue
Miami, Florida 33127

Re: K001875
Trade Name: Is-Rubella IgM Capture Test System
Regulatory Class: II
Product Code: LFX
Dated: July 19, 2000
Received: July 20, 2000

Dear Dr. Stirling:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

Attachment III

Appendix G. Indications for Use Statement

INDICATIONS FOR USE STATEMENT

510(K) NUMBER : _____

DEVICE NAME : Is-Rubella IgM Capture Test System

Indications for Use : The Diamedix Is-Rubella IgM Capture Test Kit is a capture enzyme immunoassay (EIA) for the qualitative detection of IgM antibodies to rubella in human serum as an aid in the presumptive diagnosis of current or recent infection with rubella. These reagents can be used either manually or in conjunction with the MAGO® Plus Automated EIA Processor.

Woody Dickson

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K001875

REV.